

**REMARKS/ARGUMENTS**

Claims 1-15 were pending in the instant application. The following remarks are believed to be fully responsive to the Office Action.

**THE REJECTIONS UNDER 35 U.S.C. § 103**

**SHOULD BE WITHDRAWN**

Claims 1-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Griffiths et al., WO03/059397 ("Griffiths") in view of the combined disclosures Yngve, Int. Diss. Abs. 2001, 62 ("Yngve") and Bottcher et al., and US 5,439,863 ("Bottcher") and in further view of Maier-Borst et al., GB2056471A ("Maier-Borst"). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

The present invention concerns coordination chemistry, the chemistry of complex compounds made up of a metal ion and surrounded by ligands.

Applicants refer to page 5 of the current Office Action wherein the Examiner states "the microwave synthesis technique for the method of producing metal-chelate complexes was known by Bottcher et al." Bottcher is concerned with inorganic chemistry of salts and not coordination chemistry of the instant invention. The present invention is concerned with coordination chemistry. Moreover, the instant invention deals with macromolecular bioconjugates. Bottcher studies transition metals with diketones, dithiocarbamide acid

derivatives, dihydroxy compounds, diamines and other difunctional ligands in order to use them as catalysts for polymerization and curing reactions. The instant application, however, focuses on Group 13 element, Ga(III) complexation with macrocyclic chelators naked or conjugated to macromolecules such as peptides, oligonucleotides and so on in order to improve radiopharmaceutical production. Thus, Bottcher and the present invention are as well of different classes of reactions and compounds. There is no teaching in Bottcher of applying microwave activation in coordination chemistry. The fact that no one had used microwave heating when conducting coordination chemistry using Ga clearly indicates that the usage of the microwave technique for that class of chemical reactions was absolutely not obvious.

Applicants note that “the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant’s specification, to make necessary changes in the reference device”. See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984). Furthermore, it is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). (emphasis added).

Additionally, prior art reference Maier-Borst aimed to synthesize an anion exchange resin for the separation of gallium-68 from germanium-68 thus avoiding the use of EDTA for elution as it was done before the 1980s. Its aim does not collide with our claims 1-15 and the

comparison is not relevant. In the present invention, gallium-68 is eluted from a commercial generator already in ionic form. In particular our claims 1-15 consider: i) The preconcentration of gallium-68 which is needed for the efficiency of the labeling complexing reaction. Namely, the specific radioactivity for the chelator conjugated peptide labeling was increased 200-fold. ii) The volume was decreased 30 – fold, namely, from 6 mL to 200  $\mu$ L. This makes a 30 – fold increase in peptide or any other macromolecule concentration. iii) The chelating  $^{68}\text{Ga}$ -labeling reactions are sensitive to the presence of competing metal ions therefore it is important to purify the  $^{68}\text{Ge}/^{68}\text{Ga}$  generator eluate from those elements. The ability of metal ions to form complexes with hydrochloric acid differs. The adsorbability of the negatively charged complexes of metals differs as well. Taking into account that the preconcentration procedure is based on the gallium ion ability to form  $\text{GaCl}_4^-$  complex, gallium can be purified from the competing metal ions using the anion-exchanging column.

It is therefore respectfully submitted that the 35 U.S.C. 103(a) rejections of claims 1-15 as being unpatentable over Griffiths in view of the combined disclosures Yngve and Botcher and in further view of Maier-Borst be withdrawn.

### **DOUBLE PATENTING**

Claims 1, 3-7 and 15 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 8-14 of co-pending Application No. 10/552,206. In response, Applicants submit that claims will be amended or cancelled if the instant application is indicated to be allowable.

Further, claims 1, 3-6 and 9-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8-13 of copending Application No. 11/358,681. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated to allowable.

Still further, claims 1-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 8-15, 18 and 19 of copending Application No. 10/552,206. In addition, claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 8-14 of copending Application No. 11/358,681. In response, Applicants submit that terminal disclaimers will be filed once the instant application is indicated to allowable.

**CONCLUSION**

In view of the remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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